Rejection under §112, first paragraph

The Examiner, in the last Office Action in this application, suggested that the applicants here avoid a previously imposed rejection under §112, first paragraph, by inserting a limitation the B.t. delta-endotoxins be from about 130 to 140 kD in size. This limitation was suggested to avoid an overbreadth rejection. Now the Examiner has taken the position that the specification does not support this language. Accordingly, the applicants have reworded this language in a manner, it is hoped, that results in similar claim scope but using language found in the specification.

The new language recites that the native B.t. delta-endotoxin gene produces a protein greater that 72 kD in size, and which is natively toxic upon ingestion to Manduca sexta. The specification supports both of these limitations. On page 15, line 26, the specification recites that the B.t. toxin amino terminal portion is 72 kD in size, making it clear that the native sequence must be larger yet. The toxicity of the native sequence to Manduca sexta is demonstrated in the results from the pTVAMVBTSH vector as set forth on Table I.

The scope of these two limitations, it is believed, renders the claim somewhat narrower than the language the Examiner suggested. If the Examiner refers to Table 3 of the Hofte et al. paper, it can be seen that the only identified B.t. toxin proteins which are larger than 72 kD and which are toxic to Manduca, a Lepidopteran, are the so-called cryI gene types. These are among the gene types which produce 130 to 140 kD proteins. The limitation adopted by the applicants would not cover B.t. gene types which are not toxic to Lepidopteran insects, and hence does not even cover all of the 130 to 140 kD B.t. toxins, i.e. if the toxins are not toxic to Manduca. Hence, the claims have been limited in a manner commensurate with the scope of the disclosure, as suggested by the Examiner, but now using language that has support in the specification. It is hoped that these amendments have resolved this issue.

Rejection under §103 over Prior Art

The Examiner has also rejected claims 15-19 as anticipated or obvious over a combination of three references. The three references all disclose the creation of transgenic plants which express the amino-

terminal portion of the B.t. delta-endotoxin gene so as to be toxic to insects such as Manduca sexta. At the amino acid level, is it true, the plants described in these papers produce the same protein as the plants described in the claims of this application. However, at the nucleotide level, the plants claimed in claims 15-18 differ significantly from those described in the cited references.

The Examiner has not relied on a secondary reference to bridge this gap. Instead, the Examiner observes, correctly, that the protein produced is the same. The Examiner then observes that it would have been expected by one of ordinary skill in the art that the plants expressing the claimed constructs would be toxic to insects. This is also true. From this observation, the Examiner argues that the plants of the applicants are similar to or a variant of the plants of the references. The applicant acknowledges that the plants described and claimed here are an improvement of the plants which co-inventor Barton described in the Barton et al publication. However, the applicants assert that the Examiner's logic is faulty in asserting that the claimed plants, with novel genes in them, are obvious. It is the applicants assertion that the novel DNA sequences are unobvious themselves.

The Examiner's logic in this case is similar to the logic of the Examiner in charge of the application in In re Bell, 26 USPQ 2d. 1529 (Fed. Cir. 1993). There the Examiner rejected DNA claims because the protein encoded by those claim was old. The CAFC reversed, rejecting the proposition that "the established relationship in the genetic code between a nucleic acid and the protein it encodes also makes a gene prima facie obvious over its corresponding protein." Id. at 1531. Here the Examiner has sought to reject not the native gene sequence, but an entirely artificial gene sequence based solely on similarity at the amino acid level to a native sequence. The decision in In re Bell, supra makes it clear that such logic is impermissible.

The Bell decision provides another discussion helpful here. As in the CAFC stated in the final holding in Bell, the issue of obviousness for a claim to a gene sequence is the question of whether the sequence, considered as a composition, is obivous, not whether the method by which the sequence was made was made is obvious. Here, the applicants have defined a set of novel artificial genes for the B.t. toxin that are clearly

different from the native B.t. genes. The Examiner's rejection includes no reference which teaches genes having sequences strucutrally modified similarly to those of the applicants. In essence, considering the applicants genes as a composition, as the Court has said is appropriate, there has been no demonstration of the structural obviousness of these compositions, i.e. these genes. None of the three references suggests a gene sequence like those of the applicants here. As such, the Examiner's position does not suffice to create a prima facie case for non obviousness.

It is the position of the applicants here, however, that even if a prima facie case for non obviousness had been made, that the applicants here have produced data which should rightfully overcome such a rejection. While the Examiner is correct in that it would have been expected that the plants as recited in claims 15-18 would be toxic at some level to insects, there was, in the applicants' view, insufficient guidance in the prior art to expect that the claimed plants would kill insects better that the prior art plants. The specification demonstrates that the claimed plants are, in fact, more toxic that the prior art plants. The Examiner seems to suggest that the results have to be unexpectedly or surprisingly higher before non obviousness can be found. The applicants assert that such a standard is improper and too strict. When, as here, there is not structural obviousness of the claimed compositions, and where, as here, the claimed compositions are superior to the prior art, to any degree, the novel compositions have met the test for non obviousness.

Lastly, the cited references contain no teaching or suggestions for modifications such as those made by the applicants here. There must be a suggestion for modification or a motivation for modification in the cited references before obviousness to be found. No such suggestions and no such motivation are found in the three cited papers.

Accordingly, the rejection of these claims is improper and a reconsideration of this rejection is requested.

Conclusion

Wherefore, again the Examiner is respectfully requested to revisit the merits of the specification and claims of this patent application.

It is hoped that, at a minimum, claims 1-4 and 7 should now be in allowable condition. The only ground of rejection imposed by the Examiner

has been dealt with in a manner responsive to all the stated concerns of the Examiner. It is also hoped that, upon reconsideration, the art rejection of claim s 15-19 will also be removed.

An early and favorable reply is solicited. A separate request for extension of time has been submitted so that this response will be considered as timely filed.

Respectfully submitted,

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